Efficacy and Safety of Subcutaneous and Sublingual Immunotherapy for Allergic Rhinoconjunctivitis and Asthma

Christopher R. Roxbury, MD, Sandra Y. Lin, MD*

KEYWORDS

• Subcutaneous immunotherapy • Sublingual immunotherapy • Allergic rhinitis
• Allergen-specific immunotherapy

KEY POINTS

- Allergen-specific immunotherapy is the only therapeutic option that may alter the course of allergic rhinitis and provide symptomatic relief after discontinuation of therapy.
- Immunotherapy may be offered in either subcutaneous or sublingual formulations.
- Current evidence supports subcutaneous immunotherapy as the gold standard for treatment of allergic rhinoconjunctivitis and asthma.
- Sublingual immunotherapy is found to be safe and is an effective alternative therapy for patients unable to tolerate injections, who cannot make frequent trips to the physician's office, or who desire an alternative to injection immunotherapy.

INTRODUCTION

Allergic rhinitis (AR) is caused by a type 1, IgE-mediated immediate hypersensitivity reaction in the nasal mucosa in response to inhaled environmental allergens, with prevalence estimates between 10% and 20% in US adults and slightly higher prevalence in children.[1–3] As a result, patients may experience a combination of symptoms including nasal itching, sneezing, and nasal congestion. Additionally, these patients often experience comorbid allergic conjunctivitis and asthma. Although these sequelae are not dangerous, they can have a profound impact on quality of life,

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Department of Otolaryngology–Head and Neck Surgery, Johns Hopkins University School of Medicine, 601 North Caroline Street, 6th Floor, Baltimore, MD 21287, USA
* Corresponding author. Department of Otolaryngology–Head and Neck Surgery, Johns Hopkins Outpatient Center, 601 North Caroline Street, 6th Floor, Baltimore, MD 21287.
E-mail address: slin30@jhmi.edu

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leading to decreased productivity at school and work.[4,5] Moreover, AR has been shown to have a significant financial impact in the United States, with indirect costs being estimated as high as $9.7 billion.[6] Asthma is often seen in conjunction with AR, as 62% of patients with asthma have a history of atopy.[7]

Management of AR consists of avoidance of environmental allergens, pharmacotherapy, and allergen-specific immunotherapy (AIT). Specifics of allergen avoidance and pharmacotherapy are beyond the scope of this article. Although most patients do well with avoidance measures and pharmacotherapy alone, AIT is the only definitive therapy available that may alter the natural history of disease. This therapy involves repetitive dosing of allergens in a controlled fashion, with the ultimate goal of increasing tolerance to the allergen, decreasing AR symptoms, and reducing the need for pharmacotherapy.

There are currently 2 forms of AIT available in the United States: subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT),[8] which may be offered to patients with AR symptoms and positive allergy skin testing. Compared with SCIT, which involves repeat office visits and injections, SLIT involves introduction of allergen tablets or aqueous drops under the tongue. As such, SLIT may provide a simpler and easier-to-deliver form of AIT. Although the US Food and Drug Administration has only recently approved tablet formulations of SLIT, as of 2009, up to 80% of all AIT in Europe consisted of SLIT.[9] In addition, the off-label use of aqueous SCIT allergens for SLIT in the United States has also been increasing in popularity.[10] The objective of this review is to compare subcutaneous and sublingual immunotherapy in terms of clinical efficacy and safety profile (**Table 1**).

SUBCUTANEOUS IMMUNOTHERAPY

Dosing and Patient Considerations

SCIT was first described in 1911[11] and remains the mainstay of AIT performed in the United States. Subcutaneous immunotherapy is indicated in individuals with positive allergy skin testing and allergic rhinitis with poorly controlled symptoms using maximal pharmacotherapy and in patients with coexisting allergy and asthma. Relative indications include inability to tolerate pharmacotherapy or desire to avoid the need for pharmacotherapy.[12,13]

SCIT may be performed in the setting of previous quantitative skin testing, whereby a safe starting dose of antigen is determined. The initial dose is gradually increased during the escalation phase of SCIT, in which weekly injections are performed with the goal of reaching a maintenance dose that appropriately alleviates AR symptoms without adverse effects. Maintenance doses depend on patient factors such as ability to tolerate injections and compliance. There are known ranges for effective doses of dust mite, cat, dog, pooid grasses, and ragweed allergens.[13] When an effective dose is reached, a maintenance phase of 3 to 5 years of regularly scheduled injections is typically initiated.[14]

Effectiveness

The World Allergy Organization (WAO) recommends that the minimum clinically relevant efficacy of immunotherapy be “at least 20% higher than placebo.”[15] Several randomized, controlled trials and systematic reviews assessed the efficacy of SCIT. High-grade evidence suggests that SCIT is effective in improving symptoms of asthma and rhinoconjunctivitis, decreasing asthma medication usage, and improving disease-specific quality of life in patients with rhinitis/rhinoconjunctivitis.[16–23] There is moderate evidence to suggest SCIT decreases medication use in rhinoconjunctivitis. The